

What is claimed is:

1. A method for manufacturing engineered tissue, comprising the steps of:

(A) profiling a sample of normal tissue specimens obtained from a subset of a population of subjects with shared characteristics to generate a plurality of structural indices that correspond to statistically significant representations of characteristics of tissue associated with the population, wherein the plurality of structural indices include cell density, matrix density, blood vessel density and layer thickness;

(B) forming an engineered tissue design in accordance with the structural indices generated in step (A); and

(C) manufacturing engineered tissue in accordance with the engineered tissue design.

2. The method of claim 1, wherein step (A) comprises the steps of:

(i) deriving imaging information by imaging a plurality of sections of each tissue specimen from the subset;

(ii) determining distributions of cell density values, matrix density values and blood vessel density values associated with the plurality of sections in accordance with the imaging information; and

(iii) determining a cell density index representative of tissue associated with the population in accordance with the distribution of cell density values determined in step (ii); determining a matrix density index representative of tissue associated with the population in

accordance with the distribution of matrix density values determined in step (ii); and determining a blood vessel density index representative of tissue associated with the population in accordance with the distribution of blood vessel density values determined in step (ii).

3. The method of claim 2, wherein step (A)(iii) comprises:

(iii) determining a cell density index representative of tissue associated with the population by calculating a statistical average of the distribution of cell density values determined in step (ii); determining a matrix density index representative of tissue associated with the population by calculating a statistical average of the distribution of matrix density values determined in step (ii); and determining a blood vessel density index representative of tissue associated with the population by calculating a statistical average of the distribution of blood vessel density values determined in step (ii).

4. The method of claim 3, wherein the statistical average of the distribution of cell density values corresponds to a mean, median or mode of the distribution of cell density values, the statistical average of the distribution of matrix density values corresponds to a mean, median or mode of the distribution of matrix density values, and the statistical average of the distribution of blood vessel density values corresponds to a mean, median or mode of the distribution of blood vessel density values.

5. The method of claim 4, wherein step (A)(iii) further comprises:

(iii) determining a further cell density index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of cell density values determined in step (ii); determining a further matrix density index representative

of tissue associated with the population by calculating an index of dispersion associated with the distribution of matrix density values determined in step (ii); and determining a further blood vessel density index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of blood vessel density values determined in step (ii).

6. The method of claim 5, wherein the index of dispersion associated with the distribution of cell density values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of cell density values, the index of dispersion associated with the distribution of matrix density values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of matrix density values, and the index of dispersion associated with the distribution of blood vessel density values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of blood vessel density values.

7. The method of claim 6, wherein the plurality of structural indices generated in step (A) further include relative cell location, relative matrix location, and relative blood vessel location.

8. The method of claim 7, wherein step (A)(ii) further comprises the steps of:

- (ii) determining distributions of relative cell location values, relative matrix location values and relative blood vessel location values associated with the plurality of sections in accordance with the imaging information; and

step (A)(iii) further comprises the step of:

(iii) determining a relative cell location index representative of tissue associated with the population in accordance with the distribution of relative cell location values determined in step (ii); determining a relative matrix location index representative of tissue associated with the population in accordance with the distribution of relative matrix location values determined in step (ii); and determining a relative blood vessel location index representative of tissue associated with the population in accordance with the distribution of relative blood vessel location values determined in step (ii).

9. The method of claim 8, wherein step (A)(iii) further comprises:

(iii) determining a relative cell location index representative of tissue associated with the population by calculating a statistical average of the distribution of relative cell location values determined in step (ii); determining a relative matrix location index representative of tissue associated with the population by calculating a statistical average of the distribution of relative matrix location values determined in step (ii); and determining a relative blood vessel location index representative of tissue associated with the population by calculating a statistical average of the distribution of relative blood vessel location values determined in step (ii).

10. The method of claim 9, wherein the statistical average of the distribution of relative cell location values corresponds to a mean, median or mode of the distribution of relative cell location values, the statistical average of the distribution of relative matrix location values corresponds to a mean, median or mode of the distribution of relative matrix location values, and the statistical average of the distribution of relative blood vessel location values corresponds to a mean, median or mode of the distribution of relative blood vessel location values.

11. The method of claim 10, wherein step (A)(iii) further comprises:

(iii) determining a further relative cell location index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of relative cell location values determined in step (ii); determining a further relative matrix location index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of relative matrix location values determined in step (ii); and determining a further relative blood vessel location index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of relative blood vessel location values determined in step (ii).

12. The method of claim 11, wherein the index of dispersion associated with the distribution of relative cell location values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of relative cell location values, the index of dispersion associated with the distribution of relative matrix location values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of relative matrix location values, and the index of dispersion associated with the distribution of relative blood vessel location values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of relative blood vessel location values.

13. The method of claim 12, wherein the engineered tissue design formed in step (B) includes coordinates of cells, matrices and blood vessels.

14. The method of claim 13, wherein the coordinates correspond to Cartesian coordinates.

15. The method of claim 12, wherein the imaging information is derived in step (A) using at least one imaging modality selected from the following group of imaging modalities: light microscopy, fluorescent microscopy, spectral microscopy, hyper-spectral microscopy, electron microscopy, confocal microscopy and optical coherence tomography.

16. The method of claim 15, wherein the imaging information is derived in step (A) using a combination of two or more imaging modalities selected from the following group of imaging modalities: light microscopy, fluorescent microscopy, spectral microscopy, hyper-spectral microscopy, electron microscopy, confocal microscopy and optical coherence tomography.

17. The method of claim 12, wherein the sample of normal tissue specimens corresponds to a group of normal tissue specimens associated with a specific race, sex, age, disease, physical fitness level, behavior, geographic location or nationality of persons.

18. The method of claim 17, wherein the specific race is one of the group consisting of Caucasian, Asian, Indian or Negro.

19. The method of claim 12, wherein the engineered tissue design conforms to a normal tissue structure.

20. The method of claim 19, wherein the engineered tissue design conforms to a living tissue structure.

21. The method of claim 20, wherein the population of subjects consists of a group of subjects classified in a specific animal species.

P
E
R
F
O
R
M
A
N
C
E

22. The method of claim 20, wherein the population of subjects consists of a group of subjects classified in a specific plant species.

23. The method of claim 12, wherein the engineered tissue design conforms to a virtual tissue structure.

24. The method of claim 12, wherein the normal tissue specimens from the subset of the population do not include blood vessels and the blood vessel density index generated in step (A) is zero.

25. The method of claim 12, wherein the cell density index generated in step (A) is an average cell density value associated with a specific cell type contained within the normal tissue specimens.

A

26. The method of claim 25, wherein the plurality of structural indices generated in step (A) include a plurality of average cell density values each of which is associated with a specific cell type contained within the normal tissue specimens.

27. The method of claim 12, wherein the plurality of structural indices generated in step (A) further comprise a parameter representative of average cell content within the population.

28. The method of claim 12, wherein the plurality of structural indices generated in step (A) further comprise a parameter representative of average cell type within the population.

29. The method of claim 12, wherein step (A) further comprises profiling the sample of normal tissue specimens obtained from the subset of the population with shared characteristics

to generate one or more mechanical indices that correspond to statistically significant representations of characteristics of tissue associated with the population, and step (B) comprises forming the engineered tissue design in accordance with the structural indices and the mechanical indices.

30. The method of claim 29, wherein at least one of the mechanical indices corresponds to a modulus of elasticity associated with the normal tissue specimens.

31. The method of claim 30, wherein step (A)(ii) further comprises:

(ii) determining a distribution of elasticity values associated with the plurality of sections; and

and step (A)(iii) further comprises:

(iii) determining an elasticity index representative of tissue associated with the population in accordance with the distribution of elasticity values determined in step (ii).

32. The method of claim 31, wherein step (A)(iii) further comprises:

(iii) determining an elasticity index representative of tissue associated with the population by calculating a statistical average of the distribution of elasticity values determined in step (ii).

33. The method of claim 32, wherein the statistical average of the distribution of elasticity values corresponds to a mean, median or mode of the distribution of elasticity values.

34. The method of claim 33, wherein step (A)(iii) further comprises:

(iii) determining a further elasticity index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of elasticity values determined in step (ii).

35. The method of claim 34, wherein the index of dispersion associated with the distribution of elasticity values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of elasticity values.

36. The method of claim 29, wherein at least one of the mechanical indices corresponds to a mechanical strength associated with the normal tissue specimens.

37. The method of claim 36, wherein the mechanical strength corresponds to a breaking strength associated with the normal tissue specimens.

38. The method of claim 36, wherein step (A)(ii) further comprises:

(ii) determining a distribution of mechanical strength values associated with the plurality of sections; and

and step (A)(iii) further comprises:

(iii) determining a mechanical strength index representative of tissue associated with the population in accordance with the distribution of mechanical strength values determined in step (ii).

39. The method of claim 38, wherein step (A)(iii) further comprises:

(iii) determining a mechanical strength index representative of tissue associated with the population by calculating a statistical average of the distribution of mechanical strength values determined in step (ii).

40. The method of claim 39, wherein the statistical average of the distribution of mechanical strength values corresponds to a mean, median or mode of the distribution of mechanical strength values.

41. The method of claim 40, wherein step (A)(iii) further comprises:

(iii) determining a further mechanical strength index representative of tissue associated with the population by calculating an index of dispersion associated with the distribution of mechanical strength values determined in step (ii).

42. The method of claim 41, wherein the index of dispersion associated with the distribution of mechanical strength values corresponds to a standard deviation, standard error of the mean or range associated with the distribution of mechanical strength values.

43. The method of claim 12, wherein step (A) further comprises performing a plurality of cell function assays on the sample of normal tissue specimens obtained from the subset of the population of subjects with shared characteristics and generating a plurality of cell function indices that correspond to statistically significant representations of characteristics of tissue associated with the population in accordance with results of the cell function assays, and step (B) comprises forming the engineered tissue design in accordance with the structural indices and functional indices.

44. The method of claim 43, wherein step (A) further comprises forming a cell function map in accordance with the cell function indices, and step (B) comprises forming the engineered tissue design in accordance with the cell function map.

45. The method of claim 43, wherein the cell function indices include location, type and amount of DNA in the normal tissue specimens from the subset.

46. The method of claim 43, wherein the cell function indices include location, type and amount of mRNA in the normal tissue specimens from the subset.

47. The method of claim 43, wherein the cell function indices include location, type and amount of cellular proteins in the normal tissue specimens from the subset.

48. The method of claim 43, wherein the cell function indices include location, type and amount of cellular lipids in the normal tissue specimens from the subset.

49. The method of claim 43, wherein the cell function indices include location, type and amount of cellular ion distributions in the normal tissue specimens from the subset.

50. The method of claim 13, wherein step (B) further comprises forming the engineered tissue design in accordance a correlation between two structural indices.

51. The method of claim 29, wherein step (B) further comprises forming the engineered tissue design in accordance a correlation between two mechanical indices.

52. The method of claim 43, wherein step (B) further comprises forming the engineered tissue design in accordance a correlation between two cell function indices.

3 2 0 0 3 4 0 2 0

53. The method of claim 29, wherein step (B) further comprises forming the engineered tissue design in accordance a correlation between a structural index and a mechanical index.

54. The method of claim 43, wherein step (B) further comprises forming the engineered tissue design in accordance a correlation between a structural index and a cell function index.

55. The method of claim 43, wherein step (B) further comprises forming the engineered tissue design in accordance a correlation between a mechanical index and a cell function index.

A

56. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal lung tissue specimens, and the engineered tissue design corresponds to an engineered lung tissue design.

57. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal intestine tissue specimens, and the engineered tissue design corresponds to an engineered intestine tissue design.

58. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal cartilage tissue specimens, and the engineered tissue design corresponds to an engineered cartilage tissue design.

59. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal eye tissue specimens, and the engineered tissue design corresponds to an engineered eye tissue design.

RECORDED MAIL

60. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal bone tissue specimens, and the engineered tissue design corresponds to an engineered bone tissue design.

61. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal fat tissue specimens, and the engineered tissue design corresponds to an engineered fat tissue design.

62. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal muscle tissue specimens, and the engineered tissue design corresponds to an engineered muscle tissue design.

63. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal kidney tissue specimens, and the engineered tissue design corresponds to an engineered kidney tissue design.

64. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal brain tissue specimens, and the engineered tissue design corresponds to an engineered brain tissue design.

65. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal heart tissue specimens, and the engineered tissue design corresponds to an engineered heart tissue design.

66. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal liver tissue specimens, and the engineered tissue design corresponds to an engineered liver tissue design.

0000000000000000

67. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal skin tissue specimens, and the engineered tissue design corresponds to an engineered skin tissue design.

68. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal pleura tissue specimens, and the engineered tissue design corresponds to an engineered pleura tissue design.

69. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal peritoneum tissue specimens, and the engineered tissue design corresponds to an engineered peritoneum tissue design. A

70. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal pericardium tissue specimens, and the engineered tissue design corresponds to an engineered pericardium tissue design.

71. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal dura-mater tissue specimens, and the engineered tissue design corresponds to an engineered dura-mater tissue design.

72. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal oral-nasal mucus membrane tissue specimens, and the engineered tissue design corresponds to an engineered oral-nasal mucus membrane tissue design.

73. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal pancreas tissue specimens, and the engineered tissue design corresponds to an engineered pancreas tissue design.

74. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal spleen tissue specimens, and the engineered tissue design corresponds to an engineered spleen tissue design.

75. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal gall bladder tissue specimens, and the engineered tissue design corresponds to an engineered gall bladder tissue design.

76. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal blood vessel tissue specimens, and the engineered tissue design corresponds to an engineered blood vessel tissue design.

77. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal bladder tissue specimens, and the engineered tissue design corresponds to an engineered bladder tissue design.

78. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal uterus tissue specimens, and the engineered tissue design corresponds to an engineered uterus tissue design.

79. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal ovarian tissue specimens, and the engineered tissue design corresponds to an engineered ovarian tissue design.

80. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal urethra tissue specimens, and the engineered tissue design corresponds to an engineered urethra tissue design.

0
1
2
3
4
5
6
7
8
9
A
B
C
D
E
F
G
H
I
J
K
L
M
N
O
P
Q
R
S
T
U
V
W
X
Y
Z

81. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal penile tissue specimens, and the engineered tissue design corresponds to an engineered penile tissue design.

82. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal vaginal tissue specimens, and the engineered tissue design corresponds to an engineered vaginal tissue design.

83. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal esophagus tissue specimens, and the engineered tissue design corresponds to an engineered esophagus tissue design.

A

84. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal anus tissue specimens, and the engineered tissue design corresponds to an engineered anus tissue design.

85. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal adrenal gland tissue specimens, and the engineered tissue design corresponds to an engineered adrenal gland tissue design.

86. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal ligament tissue specimens, and the engineered tissue design corresponds to an engineered ligament tissue design.

87. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal intervertebral disk tissue specimens, and the engineered tissue design corresponds to an engineered intervertebral disk tissue design.

0
1
2
3
4
5
6
7
8
9

88. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal bursa tissue specimens, and the engineered tissue design corresponds to an engineered bursa tissue design.

89. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal meniscus tissue specimens, and the engineered tissue design corresponds to an engineered meniscus tissue design.

90. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal fascia tissue specimens, and the engineered tissue design corresponds to an engineered fascia tissue design.

A

91. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal bone marrow tissue specimens, and the engineered tissue design corresponds to an engineered bone marrow tissue design.

92. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal tendon tissue specimens, and the engineered tissue design corresponds to an engineered tendon tissue design.

93. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal pulley tissue specimens, and the engineered tissue design corresponds to an engineered pulley tissue design.

94. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal tendon sheath tissue specimens, and the engineered tissue design corresponds to an engineered tendon sheath tissue design.

95. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal lymph node tissue specimens, and the engineered tissue design corresponds to an engineered lymph node tissue design.
96. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to normal nerve tissue specimens, and the engineered tissue design corresponds to an engineered nerve tissue design.
97. The method of claim 96, wherein the normal tissue specimens profiled in step (A) correspond to normal motor nerve tissue specimens, and the engineered tissue design corresponds to an engineered motor nerve tissue design.
98. The method of claim 96, wherein the normal tissue specimens profiled in step (A) correspond to normal sensory nerve tissue specimens, and the engineered tissue design corresponds to an engineered sensory nerve tissue design.
99. The method of claim 96, wherein the normal tissue specimens profiled in step (A) correspond to normal autonomic nerve tissue specimens, and the engineered tissue design corresponds to an engineered autonomic nerve tissue design.
100. The method of claim 12, wherein the normal tissue specimens profiled in step (A) correspond to first and second groups of different normal tissue specimens, wherein the first and second groups each correspond to a set of either normal intestine tissue specimens, normal cartilage tissue specimens, normal eye tissue specimens, normal bone tissue specimens, normal fat tissue specimens, normal muscle tissue specimens, normal kidney tissue specimens, normal brain tissue specimens, normal heart tissue specimens, normal liver tissue specimens, normal

skin tissue specimens, normal pleura tissue specimens, normal peritoneum tissue specimens,
normal pericardium tissue specimens, normal dura-mater tissue specimens, normal oral-nasal
mucus membrane tissue specimens, normal pancreas tissue specimens, normal spleen tissue
specimens, normal gall bladder tissue specimens, normal blood vessel tissue specimens, normal
bladder tissue specimens, normal uterus tissue specimens, normal ovarian tissue specimens,
normal urethra tissue specimens, normal penile tissue specimens, normal vaginal tissue
specimens, normal esophagus tissue specimens, normal anus tissue specimens, normal adrenal
gland tissue specimens, normal ligament tissue specimens, normal intervertebral disk tissue
specimens, normal bursa tissue specimens, normal meniscus tissue specimens, normal fascia
tissue specimens, normal bone marrow tissue specimens, normal tendon tissue specimens,
normal pulley tissue specimens, normal tendon sheath tissue specimens, normal lymph node
tissue specimens, or normal nerve tissue specimens, and the engineered tissue design
corresponds to an engineered composite tissue design.

101. The method of claim 12, wherein the engineered tissue design includes at least
one structural feature that repeats in a common fashion throughout the design.

102. The method of claim 43, wherein the engineered tissue design includes at least
one cellular function feature that repeats in a common fashion throughout the design.

103. A method for manufacturing engineered tissue, comprising the steps of:

(A) performing a plurality of cell function assays on a sample of normal tissue
specimens obtained from a subset of the population of subjects with shared characteristics and
generating a plurality of cell function indices that correspond to statistically significant

representations of characteristics of tissue associated with the population in accordance with results of the cell function assays;

(B) forming an engineered tissue design in accordance with the cell function indices; and

(C) manufacturing engineered tissue in accordance with the engineered tissue design.

104. The method of claim 103, wherein step (A) further comprises forming a cell function map in accordance with the cell function indices, and step (B) comprises forming the engineered tissue design in accordance with the cell function map.

105. The method of claim 103, wherein the cell function indices include location, type and amount of DNA in the normal tissue specimens from the subset.

106. The method of claim 103, wherein the cell function indices include location, type and amount of mRNA in the normal tissue specimens from the subset.

107. The method of claim 103, wherein the cell function indices include location, type and amount of cellular proteins in the normal tissue specimens from the subset.

108. The method of claim 103, wherein the cell function indices include location, type and amount of cellular lipids in the normal tissue specimens from the subset.

109. The method of claim 103, wherein the cell function indices include location, type and amount of cellular ion distributions in the normal tissue specimens from the subset.

110. The method of claim 103, wherein step (B) further comprises forming the engineered tissue design in accordance a correlation between two cell functional indices.

111. The method of claim 103, wherein the engineered tissue design includes at least one cellular function feature that repeats in a common fashion throughout the design.

00000000000000000000000000000000

